For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

STYPTOVIT TX

1. GENERIC NAMEF

Etamsylate & Tranexamic Acid Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Etamsylate B.P. …… 250 mg

Tranexamic Acid I.P……..250 mg

Colours: Erythrosine & Titanium Dioxide I.P.

The excipients used are Starch, Sodium Benzoate, Sodium Starch Glycolate, Magnesium Stearate, Talcum, Colloidal Silicon Dioxide, Col Erythrosine, AKOAT-512, Dibasic Calcium Phosphate, Polyvinyl Pyrrolidone.

3. DOSAGE FORM AND STRENGTH

DOSAGE: Tablet

STRENGTH: 500 mg

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Styptovit TX tablets are indicated for the treatment of abnormal blood loss due to menorrhagia, local fibrinolysis and intra operative/post-operative haemorrhage.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Dose: As directed by physician

Etamsylate

250 mg twice daily to 500mg thrice daily until bleeding stops.

In menorrhagia and metrorrhagia: 250 mg 8th hourly. Increases the dosage to 500mg 8th hourly if required depending up on the condition of the disease.

In persistent menorrhagia take 0.5g 8th hourly starting form 5 days before menstruation and continued up to 5 days after menstruation.

Children: Half of adult dose.

Tranexamic Acid

Adults:

Local Fibrinolysis: The recommended standard dose is 15-25mg/kg bodyweight (i.e. 2-3 tablets) two to three times daily. For the indications listed below the following doses may be used:

1a. Prostatectomy: Prophylaxis and treatment of haemorrhage in high risk patients should commence per- or postoperatively with an injectable form; thereafter 2 tablets three to four times daily until macroscopic haematuria is no longer present.

1b. Menorrhagia: Recommended dosage is 2 tablets 3 times daily as long as needed for up to 4 days. If very heavy menstrual bleeding, dosage may be increased. A total dose of 4g daily (8 tablets) should not be exceeded. Treatment with tranexamic acid should not be initiated until menstrual bleeding has started.

1c. Epistaxis: When repeated bleeding is anticipated oral therapy (2 tablets three times daily) should be administered for 7 days.

1d. Cervix Conisation: 3 tablets three times daily

1e. Traumatic Hyphaema: 2-3 tablets 3 times daily. The dose is based on 25mg/kg three times a day.

2. Haemophilia: In the management of dental extractions 2-3 tablets every eight hours. The dose is based on 25mg/kg.

3. Hereditary angioneurotic oedema: Some patients are aware of the onset of illness; suitable treatment for these patients is intermittently 2-3 tablets two to three times daily for some days. Other patients are treated continuously at this dosage.

Pediatric population: This should be calculated according to bodyweight at 25mg/kg per dose at the adult dosing frequencies. However, data on efficacy, posology and safety for these indications are limited.

Elderly:

No reduction in dosage is necessary unless there is evidence of renal failure (see guidelines below).

Renal insufficiency: By extrapolation from clearance data relating to the intravenous dosage form, the following reduction in the oral dosage is recommended for patients with mild to moderate renal insufficiency:

Serum Creatinine(µmol/l)	**Oral Dose**	**Dose Frequency**
120-249	15 mg/kg body weight	twice daily
250-500	15 mg/kg body weight	daily

4.3 CONTRAINDICATIONS

Etamsylate

Acute porphyria.

Hypersensitivity to the active substance or to any of the excipients.

Bronchial asthma, proven hypersesnitivity to sulphites.

Tranexamic Acid

Hypersensitivity to the active substance or to any of the excipients.

Severe renal failure because of risk of accumulation.

Active thromboembolic disease.

History of venous or arterial thrombosis

Fibrinolytic conditions following consumption coagulopathy

History of convulsions

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Etamsylate

If Etamsylate administered for a reduction of excessive and/or prolonged menstrual haemorrhages, and no improvement is observed, possible pathological causes should be looked for and excluded.

Tranexamic Acid

In case of haematuria of renal origin (especially in haemophilia), there is a risk of mechanical anuria due to formation of a ureteral clot.

In the long-term treatment of patients with hereditary angioneurotic oedema, regular eye examinations (e.g. visual acuity, slit lamp, intraocular pressure, and visual fields) and liver function tests should be performed.

Patients with irregular menstrual bleeding should not use Tranexamic Acid until the cause of irregular bleeding has been established. If menstrual bleeding is not adequately reduced by Tranexamic Acid, an alternative treatment should be considered.

Tranexamic acid should be administered with care in patients receiving oral contraceptives because of the increased risk of thrombosis.

Patients with a previous thromboembolic event and a family history of thromboembolic disease (patients with thrombophilia)

Should use Tranexamic Acid only if there is a strong medical indication and under strict medical supervision.

The blood levels are increased in patients with renal insufficiency. Therefore a dose reduction is recommended.

The use of tranexamic acid in cases of increased fibrinolysis due to disseminated intravascular coagulation is not recommended.

Patients who experience visual disturbance should be withdrawn from treatment.

Clinical experience with Tranexamic Acid in menorrhagic children under 15 years of age is not available.

4.5 DRUG INTERACTION

Etamsylate

No interaction is known up to now.

Tranexamic Acid

Tranexamic Acid will counteract the thrombolytic effect of fibrinolytic preparations.

4.6 USE IN SPECIAL POPULATION

Etamsylate

Pregnancy category C: For etamsylate, no clinical data on exposed pregnancies are available.

In reported animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/ foetal development, parturition or postnatal development. As a precaution, Etamsylate should not be administered during the first trimester of pregnancy, whereas during the second and third trimester, it should be administered only if the expected therapeutic benefit is judged as superior to the potential risk for the foetus.

In the absence of data regarding passage into maternal milk, lactation during treatment is not advisable or, if lactation is to continue, the treatment must be stopped.

Tranexamic Acid

Pregnancy

Although there is no evidence from animal studies of a teratogenic effect, the usual caution with use of drugs in pregnancy should be observed.

Tranexamic acid crosses the placenta.

Breast-feeding

Tranexamic acid passes into breast milk to a concentration of approximately one hundredth of the concentration in the maternal blood. An antifibrinolytic effect in the infant is unlikely.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

STYPTOVIT TX tablet has no effect on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS

Etamsylate

Rare: gastralgia, nausea, headache, skin rash.

In most cases, these symptoms disappear spontaneously.

If they persist, the dosage should be reduced or the treatment withdrawn.

Etamsylate contains sulphite as antioxidant that may cause allergic reactions, nausea and diarrhea in susceptible patients. The allergic reactions may lead to anaphylactic shock and cause life-threatening asthma attacks. The incidence in the population is not known but is probably low. However, hypersensitivity towards sulphite is observed more frequently in asthmatics than in nonasthmatics. In case of hypersensitivity reactions, the administration of tablets must be immediately stopped.

Tranexamic Acid

Adverse effects have been ranked under headings of frequency using the following convention:

Very common (≥ 1/10)

Common (≥1/100, <1/10)
Uncommon (≥1/1000, <1/100)
Rare (≥ 1/10,000, <1/1,000)
Very rare (<1/10,000) including isolated reports
Not known (cannot be estimated from the available data).

The following undesirable effects have been reported

Immune system disorders: Very rare: Hypersensitivity reactions including anaphylaxis

Gastrointestinal disorders: Very rare: Digestive effects such as nausea, vomiting and diarrhoea my occur but disappear when the dosage is reduced

Skin and subcutaneous tissue disorders: Rare: Allergic skin reactions.

Vascular disorders: Rare: thromboembolic events, Very rare: Arterial or venous thrombosis at any sites

Eye disorders: Rare: impaired colour vision and other visual disturbances, retinal/artery occlusion

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

4.9 OVERDOSE

Etamsylate

No case of overdose has been reported. In case of overdosage, a symptomatic treatment should be initiated.

Tranexamic Acid

Symptoms may be nausea, vomiting, orthostatic symptoms and/or hypotension. Initiate vomiting, then stomach lavage, and charcoal therapy. Maintain a high fluid intake to promote renal excretion. There is a risk of thrombosis in predisposed individuals. Anticoagulant treatment should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIESN

Etamsylate

Etamsylate is a synthetic antihaemorrhagic and angioprotective drug acting on the first step of haemostasis (endothelium-platelet interaction). By improving platelet adhesiveness and restoring capillary resistance, it is able to reduce bleeding time and blood losses.

Etamsylate has no vasoconstrictor action, it does not influence fibrinolysis nor modify the plasma coagulation factors.

Tranexamic Acid

Tranexamic acid is an antifibrinolytic compound which is a potent competitive inhibitor of the activation of plasminogen to plasmin. At much higher concentrations it is a non-competitive inhibitor of plasmin. The inhibitory effect of tranexamic acid in plasminogen activation by urokinase has been reported to be 6-100 times and by streptokinase 6-40 times greater than that of aminocaproic acid. The antifibrinolytic activity of tranexamic acid is approximately ten times greater than that of aminocaproic acid.

5.2 PHARMACOKINETIC PROPERTIES

Etamsylate

When given p.o., etamsylate is slowly absorbed from the gastrointestinal tract. After oral administration of 500 mg etamsylate maximum plasma level, i.e. 15 µg/ml, is reached at 4 h, but bioavailability is not known. The binding rate to plasma proteins is about 95%. Plasma half-life is about 3, 7 h. About 72% of the administered dose are excreted in the first 24 h-urine; the molecule is excreted unchanged. Etamsylate crosses the placental barrier.

Maternal and cord blood contains similar concentrations of etamsylate. It is not known if etamsylate is excreted in the maternal milk.

Kinetics in particular situations

It is not known if the pharmacokinetic properties of etamsylate are modified in patients suffering from renal and/or hepatic function disorders.

Tranexamic Acid

Absorption

Peak plasma Tranexamic acid concentration is obtained immediately after intravenous administration (500mg). Then concentration decreases until the 6th hour. Elimination half-life is about 3 hours.

Distribution

Tranexamic acid administered parenterally is distributed in a two compartment model. Tranexamic acid is delivered in the cell compartment and the cerebrospinal fluid with delay. The distribution volume is about 33% of the body mass.

Tranexamic acid crossed the placenta, and may reach one hundredth of the serum peak concentration in the milk of lactating women.

Elimination

Tranexamic acid is excreted in urine as unchanged compound. 90% of the administered dose is excreted by the kidney in the twelve first hours after administration (glomerular excretion without tubular reabsorption).

Following oral administration, 1.13% and 39% of the administered dose were recovered after 3 and 24 hours respectively.

Plasma concentrations are increased in patients with renal insufficiency.

6. NON-CLINICAL PROPERTIES

6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

Etamsylate

Acute and chronic toxicity studies, foetotoxicity and mutagenicity studies on etamsylate have not revealed any toxic effect.

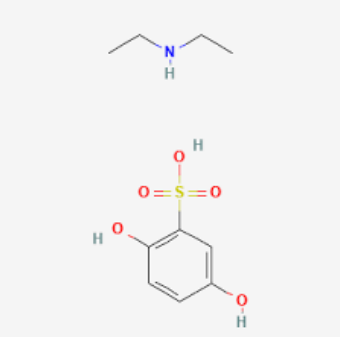
Tranexamic Acid

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics

7. DESCRIPTION

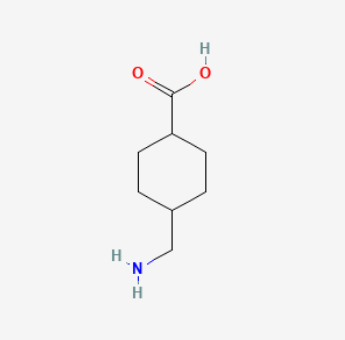
Etamsylate

Etamsylate is 2, 5-dihydroxybenzenesulfonic acid;N-ethylethanamine. The molecular formula is $C_{10}H_{17}NO_5S$ and the molecular weight is 263.31. The chemical structure of Etamsylate is:



Tranexamic Acid

Tranexamic Acid is 4-(aminomethyl) cyclohexane-1-carboxylic acid. The molecular formula is $C_8H_{15}NO_2$ and the molecular weight is 157.21. The chemical structure of Tranexamic Acid is:



STYPTOVIT TX Tablets are a pink coloured, elongated, biconvex one side scored & film coated tablets. The excipients used are Starch, Sodium Benzoate, Sodium Starch Glycolate, Magnesium Stearate, Talcum, Colloidal Silicon Dioxide, Col Erythrosine, AKOAT-512, Dibasic Calcium Phosphate, Polyvinyl Pyrrolidone.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

Not available

8.2 Shelf Life

Do not use later than date of expiry

8.3 Packaging Information

STYPTOVIT TX is available in Blister pack of 10 Tablets

8.4 Storage and handling instructions

Store protected from light and moisture at a temperature not exceeding 30°C.

9. PATIENT COUNSELLING INFORMATION

Package leaflet: Information for the user

STYPTOVIT TX

Etamsylate & Tranexamic Tablets 500mg

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• **This medicine has been prescribed for you only.** Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

9.1. What STYPTOVIT TX is and what it is used for

STYPTOVIT TX contain Etamsylate 250 mg and Tranexamic Acid 250 mg and it is used for the treatment of abnormal blood loss due to menorrhagia, local fibrinolysis and intra operative/post-operative hemorrhage

9.2. What you need to know before you take STYPTOVIT TX

Do not take STYPTOVIT TX

If you are allergic to Etamsylate or Tranexamic Acid or any of the other ingredients of this medicine;

Warnings and precautions

Talk to your doctor or pharmacist or nurse before taking STYPTOVIT TX

Etamsylate

If Etamsylate administered for a reduction of excessive and/or prolonged menstrual haemorrhages, and no improvement is observed, possible pathological causes should be looked for and excluded.

Tranexamic Acid

In case of haematuria of renal origin (especially in haemophilia), there is a risk of mechanical anuria due to formation of a ureteral clot.

In the long-term treatment of patients with hereditary angioneurotic oedema, regular eye examinations (e.g. visual acuity, slit lamp, intraocular pressure, and visual fields) and liver function tests should be performed.

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The use of tranexamic acid in cases of increased fibrinolysis due to disseminated intravascular coagulation is not recommended.

Patients who experience visual disturbance should be withdrawn from treatment.

Clinical experience with Tranexamic Acid in menorrhagic children under 15 years of age is not available.

9.3. How to take STYPTOVIT TX.

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

If you take more STYPTOVIT TX

If you take more STYPTOVIT TX, contact your doctor immediately or go to your nearest hospital. Take this package leaflet to your doctor.

If you forget to take STYPTOVIT TX

If you forget to take a dose, take your next dose at the usual time and then keep taking your medicine as told by your doctor. Do not take a double dose to make up for a forgotten dose.

If you stop taking STYPTOVIT TX

If you stop taking your medicine Please contact your doctor or pharmacist if you have any questions regarding the use of this medicinal product.

9.4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Etamsylate

Rare: gastralgia, nausea, headache, skin rash.

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Tranexamic Acid

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9.5. How to store STYPTOVIT TX

Store protected from light and moisture at a temperature not exceeding 30°C.

9.6 Contents of the pack and other information

STYPTOVIT TX is available in Blister pack of 10 tablets

The excipients used are Starch, Sodium Benzoate, Sodium Starch Glycolate, Magnesium Stearate, Talcum, Colloidal Silicon Dioxide, Col Erythrosine, AKOAT-512, Dibasic Calcium Phosphate, Polyvinyl Pyrrolidone.

10. DETAILS OF MANUFACTURER

Pure and Cure Healthcare Pvt. Ltd.

Plot No. 26A-30, Sector-8A, IIE,

SIDCUL, Ranipur, Haridwar

(Uttarakhand)- 249403

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

31/UA/2013 issued on 19.01.2017

12. DATE OF REVISION

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/STYPTOVIT TX 500 mg/Oct-23/01/PI